LXXXVII. VITAMIN D IN ADULTS.

ITS EFFECT ON THE CALCIUM AND INORGANIC PHOSPHATE OF THE BLOOD.

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Hess and Lundagen [1922] showed that in summer there is a seasonal increase of the inorganic phosphate in the blood of infants. The same phenomenon was observed in adults by Havard and Reay [1925] who found a change from 2·9 mg. per 100 cc. in winter to 4·0 mg. per 100 cc. in summer. This has been confirmed recently by Pucher [1927]. It has been suggested that this increase is due to the greater incidence of ultra-violet light during the summer months. A similar seasonal variation has been noted to occur in the serum calcium and inorganic phosphate in rabbits [Grant and Gates, 1925]. In human beings however no seasonal change in the serum calcium has been observed, and from the narrow limits within which the normal values lie it is unlikely that this should occur.

Recent work by many authors, notably Rosenheim and Webster [1927] has made it very probable that the healing of rickets by ultra-violet light, which is accompanied by a rise in the inorganic phosphate of the blood and sometimes of the calcium of the serum, is due to the formation of vitamin D from the sterols of the epidermis. This suggested that the relatively low level of the inorganic phosphate of the blood during the winter is due to a slight deficiency of vitamin D, while during the summer the level is raised owing to increased formation of vitamin D by the greater incidence of ultra-violet light. But it is difficult to accept the suggestion that vitamin D, which is concerned primarily with bone formation, should affect the calcium phosphate metabolism of adults, in whom presumably the composition of the bones is constant.

Hess and Sherman [1927] found no rise in the serum calcium after feeding irradiated cholesterol to normal adult dogs. Kultjugin [1927] irradiated rabbits with ultra-violet light and found a rise in the blood inorganic phosphate and a decrease in serum calcium. Kroetz [1927], administering irradiated ergosterol in amounts above the therapeutic dose, in human adults obtained a decrease in blood inorganic phosphate and a slight fall or no change in the serum calcium. With irradiation he found a rise in phosphate and the K/Ca ratio. The position then is clearly unsatisfactory.

Experimental.

(A). *Irradiated ergosterol feeding.*

Irradiated ergosterol was obtained in the form of "Radiostol" pellets from the British Drug Houses. Dr Underhill, of this firm, reported from feeding experiments that 1 mg. of the irradiated ergosterol from which our batch had been prepared was equivalent to more than 50 cc. of cod-liver oil.

Two experimental subjects were given 4 mg. daily, by mouth, for 11 and 13 days respectively, and a third was given 8 mg. daily for 21 days. These doses are comparable to those found by György [1927], Prinke [1927], Beumer and Falkenheim [1927] and others to be adequate in rickets. A fourth subject was kept throughout as a control. The serum calcium (Clark and Collip's modification [1925] of the Kramer-Tisdall [1921] method) and inorganic phosphate of the blood (Briggs's [1922] method) were determined daily for a control period of a week before the feeding began and daily estimations were continued during the course of the experiment. All blood samples were taken in the mornings and after not less than one hour's rest. The values varied considerably from day to day, especially in the case of the inorganic phosphate, but no significant changes in any one direction were found during the experimental period. This is shown in Table I.

Table I.

Inorganic phosphate of whole blood, and serum calcium, before and during (A) administration of irradiated ergosterol, (B) carbon-arc irradiation. (Note that the differences between the mean values for control and experimental periods are of the same order as the "probable error of the mean value" and negligible compared with the seasonal change.)

		Inorganic phosphate of whole blood					Serum calcium				
Subject	Experimental conditions	No. of determinations	Mean values mg. P per 100 cc.	Difference in mean values	Probable error of mean*	Maximum percentage range	No. of determinations	Mean values mg. Ca per 100 cc.	Difference in mean values	Probable error of mean*	Maximum percentage range
(A). *Administration of irradiated ergosterol:*											
R. E. Havard (M.)	Control period	9	2·98	0·13	0·05	23	4	9·58	0·01	0·04	2·4
	4 mg. *per diem* irradiated ergosterol	11	3·11		0·02	14	10	9·59		0·05	7·0
E. Howland (F.)	Control period	8	3·76	0·01	0·03	10	3	9·93	0·05	0·05	2·5
	4 mg. *per diem* irradiated ergosterol	12	3·77		0·03	13	11	9·88		0·05	7·7
J. O. Girsavicius (M.)	Control period	10	3·13	0·02	0·05	26	7	10·30	0·27	0·10†	9·7
	8 mg. *per diem* irradiated ergosterol	17	3·11		0·03	20	16	10·03		0·05	11·0
L. H. Stickland (M.)	Control A	9	3·16	0·04	0·05	18	4	10·06	0·40	0·21	6·6
	Control B	10	3·20		0·03	14	10	9·66		0·14	5·4
(B). *Carbon-arc irradiation:*											
R. E. Havard (M.)	Control period‡	20	3·05	0·11	0·02	23	14	9·59	Nil	0·04	7·0
	Irradiation period (16 days)	15	2·94		0·06	40	12	9·59		0·04	6·7
L. H. Stickland (M.)	Control period	19	3·18	0·09	0·02	19	14	9·81	0·13	0·05	9·8
	Irradiation period (16 days)	15	3·09		0·03	15	13	9·94		0·06	9·8

* For formula see Hill, Long and Lupton [1924].
† Several of these readings were done on 1 cc. serum with a resulting experimental error of about 3 %.
‡ This includes the period of irradiated ergosterol feeding.

(B). *Carbon-arc irradiation.*

Two subjects were irradiated daily, except on Saturdays and Sundays, for a total period of 16 days[1]. Under these conditions, this would have been sufficient to give considerable improvement in cases of clinical rickets [Hess and Unger, 1922]. General irradiation was used from three carbon-arc "white flame" lamps each about 4 ft. distant. For rickets, under these conditions, 20 minutes' exposure twice a week would have been given. In these experiments we began with 5 minutes' exposure and increased this by 5 minutes daily to a maximum of 30 minutes. Desquamation and pigmentation were produced by the end of the experiments. Daily phosphate and calcium estimations were made. No significant changes were found (see Table I).

Conclusions.

These experiments failed to demonstrate any change in the winter levels of the blood inorganic phosphate and serum calcium. It seems unlikely from these negative results that the winter level of the blood inorganic phosphate is associated with any relative lack of vitamin D in our experimental subjects. Further they cast doubt, at any rate in the case of adults, upon the accuracy of the conception that the higher value of the blood inorganic phosphate during summer is due to the increased incidence of ultra-violet light.

Summary.

1. Addition of 8 mg. per day of irradiated ergosterol to the diet of a healthy adult for 21 days during the winter caused no significant change in the blood inorganic phosphate or serum calcium.

2. Irradiation by carbon-arc lamps for a period of 16 days during winter caused no change in the blood inorganic phosphate or serum calcium.

3. Doubt is cast on the conception that the summer rise in the level of the inorganic phosphate of the blood in adults is due to increased incidence of ultra-violet light.

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